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**Hybrid random walk-linear discriminant analysis method for unwrapping quantitative phase microscopy images of biological samples.**

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**Public Summary:**

Standard algorithms for phase unwrapping often fail for interferometric quantitative phase imaging (QPI) of biological samples due to the variable morphology of these samples and the requirement to image at low light intensities to avoid phototoxicity. We describe a new algorithm combining random walk-based image segmentation with linear discriminant analysis (LDA)-based feature detection, using assumptions about the morphology of biological samples to account for phase ambiguities when standard methods have failed. We present three versions of our method: first, a method for LDA image segmentation based on a manually compiled training dataset; second, a method using a random walker (RW) algorithm informed by the assumed properties of a biological phase image; and third, an algorithm which combines LDA-based edge detection with an efficient RW algorithm. We show that the combination of LDA plus the RW algorithm gives the best overall performance with little speed penalty compared to LDA alone, and that this algorithm can be further optimized using a genetic algorithm to yield superior performance for phase unwrapping of QPI data from biological samples.

**Scientific Abstract:**

Standard algorithms for phase unwrapping often fail for interferometric quantitative phase imaging (QPI) of biological samples due to the variable morphology of these samples and the requirement to image at low light intensities to avoid phototoxicity. We describe a new algorithm combining random walk-based image segmentation with linear discriminant analysis (LDA)-based feature detection, using assumptions about the morphology of biological samples to account for phase ambiguities when standard methods have failed. We present three versions of our method: first, a method for LDA image segmentation based on a manually compiled training dataset; second, a method using a random walker (RW) algorithm informed by the assumed properties of a biological phase image; and third, an algorithm which combines LDA-based edge detection with an efficient RW algorithm. We show that the combination of LDA plus the RW algorithm gives the best overall performance with little speed penalty compared to LDA alone, and that this algorithm can be further optimized using a genetic algorithm to yield superior performance for phase unwrapping of QPI data from biological samples.

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